

## CLAIMS

1. A method which can be used for detecting and/or identifying, in a library of peptide,  
5 pseudopeptide or nonpeptide compounds, a biological extract or a purified fraction of a tissue extract, a ligand for a receptor of interest which is capable of undergoing an internalization induced by the binding of said  
10 ligand, characterized in that it comprises at least the steps consisting in:
  - expressing said receptor in a labeled form at  
15 the surface of a cell,
  - placing said cell together with said library, the biological extract and/or a purified fraction of a tissue extract containing at  
20 least one peptide, pseudopeptide or nonpeptide compound likely to be a ligand for said receptor, under conditions sufficient to allow cellular internalization of said receptor-ligand complex and
  - 25 - visualizing this internalization via the detection of the label associated with said receptor.
2. The method as claimed in claim 1, characterized in  
30 that it enables the detection of a ligand concentration of about  $10^{-8}$  M.
3. The method as claimed in claim 1 or 2,  
35 characterized in that the receptor expressed is an orphan receptor.

4. The method as claimed in claim 1 or 2, characterized in that the receptor expressed is a receptor for which the endogenous ligand is known.
- 5 5. The method as claimed in one of the preceding claims, characterized in that the receptor is labeled with an autofluorescent protein.
- 10 6. The method as claimed in one of the preceding claims, characterized in that the fluorescent protein is a protein of the family of the wild-type fluorescent protein GFP or a mutant thereof.
- 15 7. The method as claimed in one of claims 1 to 5, characterized in that the fluorescent protein is selected from the proteins EGFP, EBFP and EYFP.
- 20 8. The method as claimed in one of claims 1 to 4, characterized in that the receptor is labeled using an epitope label which can be detected by immunohistochemistry.
- 25 9. The method as claimed in claim 8, characterized in that the epitope label is selected from hemagglutinin, polyhistidine, the myc and flag proteins and viral epitopes.
- 30 10. The method as claimed in one of claims 1 to 7, characterized in that the internalization is detected by optical and/or confocal microscopy.
- 35 11. The method as claimed in one of the preceding claims, characterized in that the labeled receptor belongs to the family of 7-transmembrane domain G protein-coupled receptors, GPCRs, to the family of single-transmembrane domain tyrosine kinase receptors or to the family of cytokine receptors.

12. The method as claimed in one of the preceding  
claims, characterized in that two or more  
different receptors labeled, respectively, with  
different labels are expressed at the surface of a  
5 cell.
13. The use of a method as claimed in one of the  
preceding claims, for detecting and/or identifying  
the endogenous ligands for an orphan receptor.
- 10 14. The use of a method as claimed in one of claims 1  
to 13, for identifying novel agonists or  
antagonists for a receptor for which the  
endogenous ligand is known.
- 15 15. A ligand for a receptor of interest, identified  
using the method as claimed in one of claims 1  
to 12.